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MERCHANT & GOULD - SURMODICS
P.O. BOX 2903
MINNEAPOLIS, MN 55402

EXAMINER	
HILL, KEVIN KAI	

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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,043	OPPERMAN ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,11-16,18 and 21-62* is/are pending in the application.

4a) Of the above claim(s) *3-6,22-29,31-41 and 46-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11-16,18,21 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant has elected the invention of Group I, Claims 1-21 and 42-45, drawn to a composition comprising a compound suitable for being immobilized on support and an organic anion of Formula I: R(X)m(Y)n, and a method of forming spots of said compound on a surface.

Within Group I, Applicant has further elected the restricted subgroup structure "b" of the organic anion of Formula I: R(X)m(Y)n, wherein the anion has the Formula III, specifically the organic anion composition to be phytate.

Election of Applicant's invention(s) was made without traverse. However, the species elections were traversed.

Amendments

Applicant's response and amendments, filed February 19, 2008 to the prior Office Action is acknowledged. Applicant has cancelled Claims 2, 7-10, 17, 19-20 and 63-65, withdrawn Claims 3-6, 22-29, 31-41, 46-62, and amended Claims 1, 11, 16, 18, 42 and 43.

Claims 3-6, 22-29, 31-41, 46-62 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1, 11-16, 18, 21, 42-45 are under consideration.

The amendments to the claims do not comply with the Revised Amendment Practice of 37 CFR 1.121 (See OG Notice 23 September 2003).

§1.121 Manner of making amendments in applications.

(c) Claims. Amendments to a claim must be made by rewriting the entire claim with all changes (e.g., additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical

expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(2) When claim text with markings is required. All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of "currently amended," and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of "currently amended," or "withdrawn" if also being amended, shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as "withdrawn- currently amended."

With respect to Claim 1, the correct status of the claim "Amended", but it is not annotated as such.

With respect to Claim 30, the correct status of the claim is "Withdrawn", but it is not annotated as such.

With respect to Claim 43, Applicant presents the status of Claim 43 as "Original"; however, Claim 43 was amended in the papers filed July 30, 2007, and as such "Original" is incorrect. Furthermore, the claim has been newly amended (compare Claim 43 in the papers filed July 30, 2007 and the instant claim). Thus, the correct status of Claim 43 is "Amended".

Applicant is strongly encouraged to review the Revised Amendment Practice of 37 CFR 1.121 (See OG Notice 23 September 2003) as it pertains to the future status of the claims in response to this Office Action.

The Examiner acknowledges and has considered Applicant's exhibit, specifically Beaucage (Curr. Med. Chem. 8:1213-1244, 2001), in the papers filed February 19, 2008.

Priority

Applicant makes no claim for benefit or priority of a prior-filed application. Accordingly, the effective priority date of the instant application is granted as the filing date of the instant application, March 11, 2004.

Examiner's Note

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the February 19, 2008 response will be addressed to the extent that they apply to current rejection(s).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

1. **Claim 43 is rejected under 35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claim 43 recites the limitation "the organic anion" in reference to Claim 42. There is insufficient antecedent basis for this limitation in the claim because Claim 42 no longer recites the presence of an organic anion.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

2. **The prior rejection of Claims 1, 14 and 16 under 35 U.S.C. 102(b)** as being anticipated by Kretz (U.S. Patent No. 6,110,719) **is withdrawn** in light of Applicant's amendments to the claims. Kretz et al do not teach a buffer composition comprising phytate and a modified nucleic acid.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. **The prior rejection of Claims 1, 10-18 and 21 under 35 U.S.C. 103(a)** as being unpatentable over Kreft et al (Eur. F. Physiol. 439(Suppl): R66-67, 2000), as evidenced by Alberts et al (*Molecular Biology of the Cell, Third Edition,* Garland Publishing, New York, NY, 1994, pg 58), and Veraart et al (J. Chromatography A, 768: 307-313, 1997) **is withdrawn** in light of Applicant's amendments to Claim 1 and argument that the nucleic acids of Kreft et al are not modified to comprise an amine, sulfhydryl group, or mixture thereof.

4. **The prior rejection of Claims 1 and 14-15 under 35 U.S.C. 103(a)** as being unpatentable over Kretz (U.S. Patent No. 6,110,719) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989) **is withdrawn** in light of Applicant's amendments to the claims. Kretz et al do not teach a buffer composition comprising phytate and a modified nucleic acid.

5. **The prior rejection of Claims 42-44 and 65 under 35 U.S.C. 103(a)** as being unpatentable over Guo et al (Genome Res. 12(3):447-457, 2002) and Veraart et al (J. Chromatography A, 768: 307-313, 1997) **is withdrawn** in light of Applicant's argument that the combination of Guo et al and Veraart et al do not teach or suggest the use of phytate to produce a nucleic acid array, which the Examiner finds persuasive.

6. **The prior rejection of Claims 42 and 65 under 35 U.S.C. 103(a)** as being unpatentable over Guo et al (Genome Res. 12(3):447-457, 2002) and Veraart et al (J. Chromatography A, 768: 307-313, 1997), as applied to claims 42-44 and 65 above, and in further view of Rogers et al (Analytical Biochem. 266: 23-30, 1999) **is withdrawn** in light of the dependency upon the previous rejection above.

7. **The prior rejection of Claims 42 and 45 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Guo et al (Genome Res. 12(3):447-457, 2002), Veraart et al (J. Chromatography A, 768: 307-313, 1997) and Rogers et al (Analytical Biochem. 266: 23-30, 1999), as applied to claims 42-44 and 65 above, and in further view of Lemieux et al (* of record in IDS) **is withdrawn** in light of the dependency upon the previous rejection above.

8. **Claims 1, 11-12, 16, 18 and 21 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Beaucage et al (Curr. Med. Chem. 8:1213-1244, 2001; *of record) in view of

Guire et al (U.S. Patent 6,506,895), Veraart et al (J. Chromatography A, 768: 307-313, 1997; *of record) and Matsumoto et al (U.S. Patent 5,165,344).

Determining the scope and contents of the prior art.

Beaucage et al teach a composition comprising a modified compound suitable for being immobilized on support, wherein the modified compound comprises nucleic acid and where the nucleic acid has been modified so as to comprise an amine groups, a sulfhydryl group, or a mixture thereof. The nucleic acids to be printed onto DNA microarray formats are first functionalized according to standard phosphoroamidite chemistry, and functionalized to contain an amino group or a sulfhydryl group at either the 5'- or 3'-terminus (pg 1214, col. 2, last ¶; pg 1216, Figure 3). Beaucage et al taught an example of immobilizing functionalized nucleic acids to a support, wherein the pH of the buffer is greater than or equal to about pH 6 to about 7, and greater than or equal to about pH 7.5 (pg 1219, Figure 6; pg 1221, col. 2, line 13; Figure 11). Beaucage et al teach that photolithographic techniques have been applied by generating arrays of densely packed oligonucleotide probes on DNA chips (pg 1232, col. 2, Photolithographic), wherein the nature of the surface to which oligonucleotides are attached, its charge, hydrophobicity, and degree of solvation are all likely to influence the environment wherein oligonucleotide interactions will take place (pg 1241, col. 1).

Beaucage et al does not teach the composition to be applied to the surface to comprise RNA. However, at the time of the invention, Guire et al disclosed nucleic acid compositions to be immobilized on a support by photolithographic techniques (Abstract), wherein the nucleic acid may be DNA or RNA (col. 4, lines 25-30).

Neither Beaucage et al nor Guire et al teach a buffer composition to comprise phytate. However, at the time of the invention, Veraart et al taught the use of phytic acid with a pH buffer comprising inorganic phosphate at pH 7.5 (pg 308, col. 2, ¶2.4.1). Veraart et al taught that phytic acid is a large, polyionic molecule whose ionic strength is relatively large as compared with its concentration (pg 307, col. 2, lines 7-11).

Neither Beaucage et al, Guire et al nor Veraart et la teach the use of phytate in a composition comprising a modified compound suitable for being immobilized on a support. However, at the time of the invention, Matsumoto et al disclosed a dampening water composition for lithographic printing which comprises a pH-buffering compound, e.g. phytate (col. 3, line 40), wherein those of ordinary skill in the art recognize phytate to be an organic anion, in an amount to effect proper etching of the support surface (col. 3, lines 32-35), wherein the pH is in a range greater than or equal to about pH 3 to 7, or if desired in the more alkaline range, pH 7 to 11 (col. 3, line 52-55). Matsumoto et al disclose the dampening water composition comprising phytate may also comprise an anionic or nonionic surfactant (col. 3, lines 58-61; col. 4, lines 20-21).

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in formulating compositions suitable for being immobilized on a support and printing means of nucleic acid arrays. Therefore, the level of ordinary skill in this art is high.

The recitation in Claim 1 "for reducing spot size when spotted onto a support" is considered an intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. The phrases "for reducing spot size when spotted onto a support" and "being effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300μm diameter on a support" are intended use limitation, which does not contain any further structural limitations with respect to claimed buffer composition comprising phytate and a functionalized nucleic acid suitable for being immobilized on a support (see MPEP §2114).

The recitation in Claim 1 "being effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300μm diameter on a support" is considered an

inherent property phytate. The prior art taught the use of phytate to improve image quality and reduce scumming when printing spots of a compound on a surface, and thus one of ordinary skill in the art would recognize that the such features would naturally flow from the use of a buffer composition comprising phytate.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to combine a composition comprising a functionalized nucleic acid suitable for being immobilized on a support with phytate with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

An artisan would be motivated to combine a composition comprising a functionalized nucleic acid suitable for being immobilized on a support with phytate because the ordinary artisan has long used phytate in methods of lithographic printing—an art-recognized means of fabricating nucleic acid microarrays—to reduce "image scumming", phytic acid has a relatively large ionic strength as compared with its concentration (Veraart et al; pg 307, col. 2, lines 7-11), and the art recognizes that increasing ionic strength can reduce non-specific adsorption to a support (Veraart et al; pg 307, column 1). The availability of twelve acidic groups with pKa values ranging from 1.9-9.5 provides the possibility to use phytic acid not only as an additive to suppress wall adsorption effects, but also to control the pH (Veraart et al; pg 308, column 1, lines 4-8). Furthermore, large, polyionic molecules are preferable because they provide high ionic strengths at relatively low currents (Veraart et al; pg 307, joining ¶). With relatively small ions used to enhance the ionic strength, the associated increment of the electric current is rather dramatic, resulting in the Joule heating effect. The Joule heating effect extant in piezoelectric delivery devices would be minimized in the presence of phytic acid, thus minimizing or avoiding unwanted heating of the composition that is to be deposited onto the support.

Thus, the invention as a whole is *prima facie* obvious.

9. **Claim 13 is rejected under 35 U.S.C. 103(a)** as being unpatentable over Beaucage et al (Curr. Med. Chem. 8:1213-1244, 2001; of record) in view of Guire et al (U.S. Patent 6,506,895), Veraart et al (J. Chromatography A, 768: 307-313, 1997; *of record) and Matsumoto et al (U.S. Patent 5,165,344) as applied to Claims 1, 11-12, 16, 18 and 21 above, and in further view of Xu et al (J. Materials Chemistry 13:3044-3048, 2003), as evidenced by Sambrook et al (Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989; SDS).

Determining the scope and contents of the prior art.

Neither Beaucage et al, Guire et al, Veraart et al nor Matsumoto et al teach the composition to comprise the anionic surfactant sodium dodecyl sulfate. However, at the time of the invention, Xu et al taught the coupling of dodecyl surfactants to nucleic acids to be immobilized on a support, whereby the surfactant anchoring group allows DNA-strands to be immobilized on hydrophobic surfaces (Abstract; Figure 1). The microcontact printing method is adapted for aqueous "inks" containing the DNA-surfactant compounds.

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in formulating compositions suitable for being immobilized on a support and printing means of nucleic acid arrays. Therefore, the level of ordinary skill in this art is high.

Xu et al do not teach the use of the anionic surfactant sodium dodecyl sulfate (SDS) specifically. However, those of ordinary skill in the art have long used SDS in combination with nucleic acids (as evidenced by Sambrook) and the structure of SDS clearly indicates ready coupling to a functionalized nucleic acid comprising sulfhydryl groups.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to modify the composition suitable for being immobilized on a support to further comprise an anionic surfactant such as sodium dodecyl sulfate (SDS) with a reasonable expectation of success because Xu et al teach the coupling of dodecyl surfactants to nucleic acids for immobilization onto a support in a method of printing nucleic acid microarrays. An artisan would be motivated to use SDS because Xu et al suggest that the main advantage of the DNA-surfactant technology is that it provides a simple way for attaching DNA strands by adhesion to a hydrophobic surface and also allows functionalization of liquid surfaces of DNA.

Thus, the invention as a whole is *prima facie* obvious.

10. **Claims 14-15 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Beaucage et al (Curr. Med. Chem. 8:1213-1244, 2001; of record) in view of Guire et al (U.S. Patent 6,506,895), Veraart et al (J. Chromatography A, 768: 307-313, 1997; *of record), Matsumoto et al (U.S. Patent 5,165,344) and Xu et al (J. Materials Chemistry 13:3044-3048, 2003), as evidenced by Sambrook et al (Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989; SDS), as applied to Claims 1, 11-13, 16, 18 and 21 above, and in further view of Yoshida (U.S. Patent 4,734,132) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989; Phosphate Buffers; *of record).

Determining the scope and contents of the prior art.

Neither Beaucage et al, Guire et al, Veraart et al, Matsumoto et al nor Xu et al teach the composition to comprise inorganic phosphate. However, at the time of the invention, Yoshida disclosed a lipophobicating solution for off-set printing which comprises phytate and a pH adjustor (Abstract), wherein the lipophobicating solution does not cause scumming and its effects last for a long period of time. Yoshida disclosed that phytate is non-toxic and facilitates pH adjustment (col. 1, lines 23-26), wherein the pH may be adjusted with sodium phosphate (col. 3, Example 1).

Neither Beaucage et al, Guire et al, Veraart et al, Matsumoto et al, Xu et al nor Yoshida teach the composition to comprise inorganic phosphate, wherein the inorganic phosphate

comprises about 10 to about 200mM sodium or potassium phosphate at pH of about 7 to about 10. However, at the time of the invention, Sambrook et al taught how an artisan may create phosphate buffered solutions using sodium phosphate and/or potassium phosphate (pg B.21, Tables B.10 and B.11; see also pg B.12 for recipe).

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in formulating compositions suitable for being immobilized on a support, printing means of nucleic acid arrays, and making buffered solutions. Therefore, the level of ordinary skill in this art is high.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to combine a buffer composition comprising phytate and a composition suitable for being immobilized on a support with an inorganic phosphate with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. At the time of the invention, those of ordinary skill in the art practiced buffering phytate compositions with inorganic phosphate and possessed formulation tables to create sodium or potassium phosphate buffered solutions, as taught by Sambrook et al, the motivation to combine because the phosphate buffer would provide a greater amount of inorganic phosphate groups into the composition and enhance the activity and buffering capacity of the phytic acid, thereby achieving their common known purpose.

Thus, the invention as a whole is *prima facie* obvious.

11. **Claims 42-45 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Bruhn et al (U.S. Patent 6,458,583) in view of Beaucage et al (Curr. Med. Chem. 8:1213-1244, 2001; *of record), Matsumoto et al (U.S. Patent 5,165,344), as evidenced by Leming Shi (DNA Microarray (Genome Chip)—Monitoring the Genome on a Chip, web.archive.org/web/20020121231509/http://www.gene-chips.com/GeneChips.html, last updated on January 7, 2002).

Determining the scope and contents of the prior art.

Bruhn et al disclose a method of forming spots of a compound on a surface, the method comprising i) applying to the surface a composition comprising a modified compound suitable for being immobilized on the surface, wherein the modified compound comprises nucleic acid and wherein the nucleic acid has been modified, and ii) forming a spot on the surface. The printing solution may comprise additional agents such as a pH buffering agent and surfactants (col. 4, lines 10-25).

Bruhn et al disclose the method to comprise the use of a thermal inkjet device to "print" or immobilize the nucleic acids onto a surface, wherein the nucleic acids may be immobilized on a variety of different substrates (col. 6, lines 41-51), and the spot size diameters can be controlled such that spots of various sizes can be produced, e.g. ranging from 10μm to 1mm, more usually from about 10μm to 200μm (col. 6, lines 15-21). The nucleic acid composition will comprise a liquid carrier that serves as a solvent, the liquid carrier further comprising pH buffering agents and surfactants (col. 4, lines 10-25).

Bruhn et al disclose that automated thermal inkjet devices to immobilize functionalized nucleic acids onto a support are analogous to conventional thermal inkjet printing devices, with the exception that the thermal inkjet head of the device is filled with a nucleic acid fluid instead of ink (col. 8, lines 1-5).

Bruhn et al do not disclose the nucleic acid to have been modified so as to comprise an amine group, a sulfhydryl group, or a mixture thereof. However, at the time of the invention, Beaucage et al taught that nucleic acids to be printed onto DNA microarray formats are first functionalized according to standard phosphoroamidite chemistry, and functionalized to contain an amino group or a sulfhydryl group at either the 5'- or 3'-terminus (pg 1214, col. 2, last ¶; pg

1216, Figure 3). Beaucage et al taught an example of immobilizing functionalized nucleic acids to a support, wherein the pH of the buffer is greater than or equal to about pH 6 to about 7, and greater than or equal to about pH 7.5 (pg 1219, Figure 6; pg 1221, col. 2, line 13; Figure 11). Beaucage et al taught that photolithographic techniques have been applied by generating arrays of densely packed oligonucleotide probes on DNA chips (pg 1232, col. 2, Photolithographic), wherein the nature of the surface to which oligonucleotides are attached, its charge, hydrophobicity, and degree of solvation are all likely to influence the environment wherein oligonucleotide interactions will take place (pg 1241, col. 1).

Neither Bruhn et al nor Beaucage et al disclose the composition applied to the surface to comprise phytate; however, at the time of the invention, Matsumoto et al disclosed a dampening water composition for lithographic printing which comprises a pH-buffering compound, e.g. phytate (col. 3, line 40), wherein those of ordinary skill in the art recognize phytate to be an organic anion, in an amount to effect proper etching of the support surface (col. 3, lines 32-35), wherein the pH is in a range greater than or equal to about pH 3 to 7, or if desired in the more alkaline range, pH 7 to 11 (col. 3, line 52-55).

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in printing means and fabrication of nucleic acid arrays. Therefore, the level of ordinary skill in this art is high.

At the time of the invention, those of ordinary skill in the art recognized that nucleic acid arrays are commonly fabricated by means of photolithography, inkjet (piezoelectric spotting), off-set printing, and drop-touch (pin spotting), wherein the sample spot sizes are typically less than 200μm in diameter (Leming Shi). Thus, the ordinary artisan could have substituted one known means of fabricating a nucleic acid array with another known means of fabricating a nucleic acid array, and the results of the substitution would have been predictable.

Neither Bruhn et al, Beaucage et al nor Matsumoto et al teach that the organic anion phytate is effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300μm diameter on a support. However, absent evidence to the contrary, one of ordinary skill in the art would recognize that the such features would naturally flow from the use of phytate to improve image quality and reduce scumming when printing spots of a compound on a surface.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to combine a composition comprising a modified compound suitable for being immobilized on the surface as taught by Bruhn et al with phytate as taught by Matsumoto et al in a method of forming spots of a compound on a surface with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. At the time of the invention, those of ordinary skill in the art practiced the use of phytate-containing buffers to reduce the scumming and improve the image [spot] quality when printing spots of a compound on a surface, e.g. by lithographic or offset printing. An artisan would be motivated to combine a composition comprising a modified compound suitable for being immobilized on the surface as taught by Bruhn et al with phytate as taught by Matsumoto et al in a method of forming spots of a compound on a surface because the ordinary artisan has long used phytate in methods of lithographic printing—an art-recognized means of fabricating nucleic acid microarrays—to reduce "image scumming", phytic acid has a relatively large ionic strength as compared with its concentration, and the art recognizes that increasing ionic strength can reduce non-specific adsorption to a support, and thus the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose.

Thus, the invention as a whole is *prima facie* obvious.

Conclusions

12. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill, Ph.D./

Examiner, Art Unit 1633

/Q. JANICE LI, M.D./
Primary Examiner, Art Unit 1633